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                     Welcome to STN International
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NEWS
                 Web Page for STN Seminar Schedule - N. America
                 CAS REGISTRY enhanced with new experimental property tags
NEWS
         AUG 06
NEWS
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         AUG 06
                 FSTA enhanced with new thesaurus edition
NEWS
         AUG 13
                 CA/CAplus enhanced with additional kind codes for granted
                 patents
NEWS
         AUG 20
                 CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS
         AUG 27
                 Full-text patent databases enhanced with predefined
                 patent family display formats from INPADOCDB
NEWS
      7
         AUG 27
                 USPATOLD now available on STN
NEWS 8
         AUG 28
                 CAS REGISTRY enhanced with additional experimental
                 spectral property data
NEWS 9
         SEP 07
                 STN AnaVist, Version 2.0, now available with Derwent
                 World Patents Index
NEWS 10
         SEP 13
                 FORIS renamed to SOFIS
NEWS 11
         SEP 13
                 INPADOCDB enhanced with monthly SDI frequency
         SEP 17
NEWS 12
                 CA/CAplus enhanced with printed CA page images from
                 1967-1998
NEWS 13
         SEP 17
                 CAplus coverage extended to include traditional medicine
NEWS 14
         SEP 24
                 EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 15 OCT 02 CA/CAplus enhanced with pre-1907 records from Chemisches
                 Zentralblatt
NEWS 16 OCT 19
                 BEILSTEIN updated with new compounds
NEWS 17 NOV 15
                 Derwent Indian patent publication number format enhanced
NEWS 18 NOV 19 WPIX enhanced with XML display format
NEWS 19 NOV 30 ICSD reloaded with enhancements
NEWS 20 DEC 04 LINPADOCDB now available on STN
NEWS 21 DEC 14 BEILSTEIN pricing structure to change
NEWS 22 DEC 17
                 USPATOLD added to additional database clusters
NEWS 23
         DEC 17
                 IMSDRUGCONF removed from database clusters and STN
NEWS 24
         DEC 17
                 DGENE now includes more than 10 million sequences
NEWS 25
         DEC 17
                 TOXCENTER enhanced with 2008 MeSH vocabulary in
                 MEDLINE segment
         DEC 17
NEWS 26
                 MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 27
         DEC 17
                 CA/CAplus enhanced with new custom IPC display formats
NEWS 28
         DEC 17
                 STN Viewer enhanced with full-text patent content
                 from USPATOLD
                 STN pricing information for 2008 now available
NEWS 29
         JAN 02
NEWS 30
         JAN 16
                 CAS patent coverage enhanced to include exemplified
                 prophetic substances
NEWS 31 JAN 28
                 USPATFULL, USPAT2, and USPATOLD enhanced with new
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custom IPC display formats

NEWS 32 JAN 28 MARPAT searching enhanced

NEWS 33 JAN 28 USGENE now provides USPTO sequence data within 3 days

of publication

NEWS 34 JAN 28 TOXCENTER enhanced with reloaded MEDLINE segment

NEWS 35 JAN 28 MEDLINE and LMEDLINE reloaded with enhancements

NEWS 36 FEB 08 STN Express, Version 8.3, now available

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3, AND CURRENT DISCOVER FILE IS DATED 24 JANUARY 2008

NEWS HOURS STN Operating Hours Plus Help Desk Availability

NEWS LOGIN Welcome Banner and News Items

NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 10:59:57 ON 14 FEB 2008

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Choice (Y/n):

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=> FILE REGISTRY

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST

0.21 0.21

FILE 'REGISTRY' ENTERED AT 11:00:26 ON 14 FEB 2008 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2008 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 13 FEB 2008 HIGHEST RN 1003293-96-6 DICTIONARY FILE UPDATES: 13 FEB 2008 HIGHEST RN 1003293-96-6 New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>

Uploading C:\Program Files\Stnexp\Queries\10560771.str

```
chain nodes :
12  13  14  15
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  16  17  18
chain bonds :
4-13  9-12  12-13  12-15  13-14
ring bonds :
1-2  1-5  2-3  3-4  4-5  6-7  6-11  6-18  7-8  7-16  8-9  9-10  10-11  16-17  17-18
```

exact/norm bonds:  $1-2 \quad 1-5 \quad 2-3 \quad 3-4 \quad 4-5 \quad 4-13 \quad 6-7 \quad 6-11 \quad 6-18 \quad 7-8 \quad 7-16 \quad 8-9 \quad 9-10 \quad 9-12 \quad 10-11 \\ 12-13 \quad 12-15 \quad 13-14 \quad 16-17 \quad 17-18$ 

isolated ring systems :
containing 1 : 6 :

G1:0, S, N, NH

G2:CH2,CH,CF2,CF3

G3:CH2,CF2,CF3,SO2,SO3H,S

Match level :

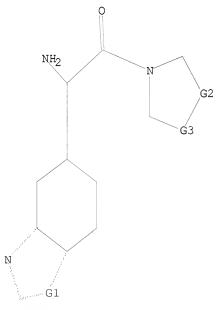
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:Atom 17:Atom 18:Atom

## L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

L1 STR



G1 O, S, N, NH

G2 CH2, CH, CF2, CF3

G3 CH2, CF2, CF3, SO2, SO3H, S

Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 11:00:48 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED -9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 9 TO 360 PROJECTED ANSWERS: 0 TO 0

L20 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 11:00:55 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 161 TO ITERATE

100.0% PROCESSED 161 ITERATIONS 7 ANSWERS

SEARCH TIME: 00.00.01

7 SEA SSS FUL L1 L3

=> FIL HCAPLUS

LNTRY SESSION 178.36 COST IN U.S. DOLLARS SINCE FILE

FULL ESTIMATED COST

FILE 'HCAPLUS' ENTERED AT 11:01:00 ON 14 FEB 2008 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 14 Feb 2008 VOL 148 ISS 7 FILE LAST UPDATED: 13 Feb 2008 (20080213/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13

5 L3 L4

=> s 14 and py<=2003

23976331 PY<=2003

L55 L4 AND PY<=2003

=> d 14 ibib abs hitstr tot

ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:2864 HCAPLUS

DOCUMENT NUMBER: 140:59935

TITLE: Preparation of crystalline (R)-2-(4-

amidinophenylaminomethyl)-1-methyl-5-(1-

(carboxymethylamino) -1 (pyrrolidinocarbonyl) -ethyl) -

benzimidazole esters and/or salts for use as

antithrombotic agents

INVENTOR(S): Linz, Guenter; Sieger, Peter; Schreiner, Gunnar; Rall,

Werner; Schmid, Rolf

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Gmbh & Co. Kg, Germany

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION: DATENT NO

PA:	PATENT NO.					)	DATE				LICAT				D	ATE	
WO	2004	0008	 18		A1	_	2003	1231			 2003-				2	0030	 616
	₩:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ,	BA,	ВВ	, BG,	BR,	BY,	BZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC	, EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE	, KG,	KP,	KR,	KΖ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN	, MW,	MX,	MZ,	NI,	NO,	NZ,	OM,
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		FΙ,	FR,	GB,	GR,	HU,	ΙE,	ΙΤ,	LU,	MC	, NL,	PT,	RO,	SE,	SI,	SK,	TR,
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ	, GW,	ML,	MR,	NE,	SN,	TD,	TG
DE	1022	7666			A1		2004	0108		DΕ	2002-	1022	7666		2	0020	620
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EP	1529	035			A1		2005	0511		EΡ	2003-	7356	29		2	0030	616
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		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL	, TR,	BG,	CZ,	EE,	HU,	SK	
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	7169						2007										
US	2007	0999	74		A1		2007	0503		US	2006-	6101	87		2	0061	213
US	7294	721			В2		2007	1113									
RIORIT	Y APP	LN.	INFO	.:							2002-					0020	
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											2003-						
										US	2003-	4630	33		A3 2	0030	617
THER SO	URCE	(S):			MARI	PAT	140:	5993	<u> </u>								

MARPAT 140:59935 OTHER SOURCE(S):

The invention relates to the crystalline forms of compds. (R)-2-(4amidinophenylaminomethyl)-1-methyl-5-(1-(carboxymethylamino)-1-(pyrrolidinocarbonyl)-ethyl)-benzimidazole and monohydrochloride thereof, to methods for the production thereof, and to their use as medicaments having an antithrombotic action (no data). Thus, (R)-2-(4cyanophenylaminomethyl)-1-methyl-5-[1-amino-1-(pyrrolidineocarbonyl)-ethyl]benzimidazole was simultaneously N-alkylated and CN-reduced/aminated using BrCH2C(0)OCH2CH2CH3 in N-methylpyyolidinone, Pr acetate, and diisopropyethylamine; the resulting ester product was first isolated as the hydrochloride, and then as the 4-toluenesulfonic acid salt, which was deesterified to give the free base. The Et ester was similarly prepared Crystal structure data were given for the free base and the monohydrochloride forms.

IT 253797-00-1

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation and x-ray crystallog. structure of 2-(4-amidinophenylaminomethyl))-1-methyl-5-(1-(carboxymethylamino)benzimidaz ole esters and/or salts for use as antithrombotic agents)

RN 253797-00-1 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:2693 HCAPLUS

DOCUMENT NUMBER: 140:53413

TITLE: Benzimidazole derivatives for the treatment of

systemic inflammatory response syndrome Ries, Uwe; Wienen, Wolfgang; Schuly, Uwe

PATENT ASSIGNEE(S): Boehringer Ingelheim, Germany

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

INVENTOR(S):

PATENT NO	).		KIN	D	DATE			APPL	ICAT	ION I	NO.		D	ATE	
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WO 200400	00310		Α1		2003	1231		WO 2	003–:	EP63	18		2	0030	616
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C	CO, CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FΙ,	GB,	GD,	GE,	GH,
G	SM, HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	KΖ,	LC,	LK,	LR,
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P	PH, PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	ΤJ,	TM,	TN,	TR,	TT,
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                                                                      20030616
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                                 20040106
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     EP 1517687
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     US 2004023975
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PRIORITY APPLN. INFO .:
                                              DE 2002-10227668
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                                                                   Α
                                              US 2002-400166P
                                                                   P
                                                                      20020801
                                              WO 2003-EP6318
                                                                      20030616
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OTHER SOURCE(S): MARPAT 140:53413

AB The invention discloses the use of benzimidazole derivs. for producing a medicament used for treating the systemic inflammatory response syndrome and particularly sepsis. Preparation of (R)-2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(carboxymethylamino)-1-(pyrrolidinocarbonyl)ethyl]benzimidazol e hydrochloride is described.

IT 253797-00-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(benzimidazole derivs. for treatment of systemic inflammatory response syndrome)

RN 253797-00-1 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:467997 HCAPLUS

DOCUMENT NUMBER: 135:61338

TITLE: Preparation of 2-(4-amidinophenylaminomethyl)benzimida

zoles as antithrombotics

INVENTOR(S): Ries, Uwe; Kauffmann, Iris; Hauel, Norbert; Priepke,

Henning; Nar, Herbert; Stassen, Jean Marie; Wienen,

Wolfgang

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: Ger. Offen., 28 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent LANGUAGE: German FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA.	TENT :		KIN	D	DATE			APE	PLI	CAT	ION I	NO.		Γ	ATE			
US	1996 2001 6451	0069	77		A1		2001 2001 2002	0705						2329 59			.9991 2 <b>0</b> 001	
	2393									CA	200	00-2	2393	916		2	0001	216
WO	2001	0478	96		A1		2001	0705		WO	200	0 0 <b>–</b> I	EP12	841		2	0001	216
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US	6593	355			В2		2003	0715										
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										US	200	00-1	1751	63P		P 2	0000	107
										US	200	00-	7351.	59			0001	
										WO	200	0 O -I	EP12	841		W 2	0001	216
OBITED OF	COUDCE (C).					_ v	100	C122	$\circ$									

OTHER SOURCE(S): MARPAT 135:61338 GI

AB Title compds. [I; R1 = alkyl, fluoroalkyl, pyrrolidinocarbonylalkyl, 2,5-dihydropyrrolocarbonylalkyl, aminoalkyl, etc., R2 = alkyl; R3 = carbamidoyl, cyano, (substituted) oxadiazolyl, etc.] and stereoisomerics thereof were prepared .Thus, (R)-2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(ethoxycarbonylmethylamino)-1-[(R,S)-2-methylpyrrolidinocarbonyl]ethyl] benzimidazole dihydrochloride in H2O was stirred with NaOH for 45 min. at room temperature followed by addition of HCl up to pH = 3.5 to give 100% (R)-2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(carboxymethylamino)-1-[(R,S)-2-methylpyrrolidinocarbonyl]ethyl]benzimidazole dihydrochloride. Several I extended (doubled) the activated partial thromboplastin time (aPTT) with ED200 = 0.12-0.22  $\mu \rm M$ .

IT 253797-00-1P 345957-57-5P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation of amidinophenylaminomethylbenzimidazoles as antithrombotics)

RN 253797-00-1 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 345957-57-5 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[1-methyl-2-[[[4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]amino]methyl]-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:34881 HCAPLUS

DOCUMENT NUMBER: 132:78556

TITLE: Preparation of amidinophenylaminomethylenzimidazoles

as antithrombotics.

INVENTOR(S): Ries, Uwe; Kauffmann, Iris; Hauel, Norbert; Priepke,

Henning; Nar, Herbert; Stassen, Jean Marie; Wienen,

Wolfgang

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 140 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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WO	20000	0170	04		A2					WO	199	99-E	EP453	31			19990	701
WO	20000						2000											
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_	23378				A1		2000	0113		CA	199	99-2	23378	304			19990	701
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	76309				A1 A1 A B2		2003	0710										
	99118				А		2001										19990	
	10950				A2		2001			ΕP	199	99-9	3276	55			19990	701
EP	10950				В1		2002											
	R:	•						FR,	GB,	GF	₹, ]	ΙΤ,	LI,	LU,	NL,	SE	, MC,	PT,
		ΙE,	SI,	LT,	LV,	FI,	RO											
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EE	4236				В1		2004											
JP	20025	51942	29		$\mathbf{T}$		2002							)6			19990	
AT	22951	11			${f T}$		2002										19990	
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IN	2000E 2000E 20010 10511	1N00	760		A		2007			ΙN	200	<b>1−</b> 00	1N760	25 319 0			20001	
ИО	20010	00002	28		A		2001			ИО	200	01-2	28				20010	
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	20010						2001			HR	200	01-7	7				20010	103
	20010				В1		2003											
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										DΕ	199	98-1	L985	7202		A	19981	211
										DΕ	199	99-1	L9912	7202 2690 31		A	19990	
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OTHER SO	OTHER SOURCE(S):						132:	78556	6									

OTHER SOURCE(S): MARPAT 132:78556

Ι

AB Title compds. [I; Ar = (substituted) phenylene, naphthylene, thienylene, thiazolylene, pyridinylene, pyrazinylene, pyrimidinylene, pyridazinylene; A = alkylene; B = O, S, CH2, CO, imino, SO, SO2; R2 = R1COX, etc.; R1 = alkoxy, amino, alkylamino, dialkylamino, etc.; X = cycloalkylene; R3 = H, alkyl; R4 = cyano, (substituted) amidino], were prepared Thus, 2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(pyrrolidin-1-ylcarbonyl)cyclopropyl]benzimidazole hydrochloride (multistep preparation

given) showed aPTT (partial thrombin time) ED200 = 0.12  $\mu M$ .

IT 253430-83-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amidinophenylaminomethylenzimidazoles as antithrombotics)

RN 253430-83-0 HCAPLUS

CN Pyrrolidine, 1-[amino[2-[[[4-(aminoiminomethyl)phenyl]amino]methyl]-1-methyl-1H-benzimidazol-5-yl]acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

# ● HCl

IT 253431-62-8P 253431-65-1P 253796-87-1P 253797-00-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amidinophenylaminomethylenzimidazoles as antithrombotics)

RN 253431-62-8 HCAPLUS

CN Pyrrolidine, 1-[amino[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]acetyl]- (9CI) (CA INDEX NAME)

RN 253431-65-1 HCAPLUS

CN Pyrrolidine, 1-[2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{O} & \text{Me} \\ \hline \\ \text{N} & \text{C} & \text{C} \\ \hline \\ \text{H}_2 \text{N} & \text{N} \end{array}$$

RN 253796-87-1 HCAPLUS

CN Pyrrolidine, 1-[2-amino-2-[1-methyl-2-[[[4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]amino]methyl]-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

RN 253797-00-1 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:15648 HCAPLUS

DOCUMENT NUMBER: 132:64257

TITLE: Preparation of amidinophenylaminomethylbenzimidazoles

and related compounds as antithrombotics.

INVENTOR(S): Ries, Uwe; Kauffmann, Iris; Hauel, Norbert; Priepke,

Henning; Nar, Herbert; Stassen, Jean Marie; Wienen,

Wolfgang

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: Ger. Offen., 38 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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	19829 6248				A1 B1	_		0105 0619		IIS	10	999-	3389	 9964 70		1	 9980 9990	
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							KΖ,					,	,					
							PL,						SE,	SG,	SI,	SK,	SL,	ТJ,
	Dir	TM,	,				UZ,						2 00	DII	011	017	D.	DII
	RW:						SD,								•	•	•	
							IE, ML,							SE,	Dr,	DU,	Cr,	CG,
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	76309				B2			0710		AU	1.		<del>-</del> 703	J		_	<i>J J J U</i>	701
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														2690			9990	
OTHER S	THER SOURCE(S):				MARI	PAT	132:	6425		WU	12	フフフー	EP45	JΙ		MA T	9990	/01

OTHER SOURCE(S): MARPAT 132:6425

AB Title compds. [I; Ar = (substituted) phenylene, naphthylene, thienylene, thiazolylene, pyridinylene, etc.; A = alkylene; B = O, S, CH2, CO, imino, sulfinyl, sulfonyl, etc.; R5 = R1COX; X = cycloalkylene; R1 = (substituted) (di)alkylamino, cycloalkyleneimino, morpholino, piperazino; R5 = H, alkyl; R7 = cyano, (substituted) amidino], were prepared Thus, 2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(pyrrolidin-1-ylcarbonyl)cyclopropyl]benzimidazole hydrochloride [prepared starting from 1-(4-chlorophenyl)-1-cyclopropanecarboxylic acid] showed aPTT (partial thrombin time) ED200 = 0.12 μM.

IT 253430-83-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amidinophenylaminomethylbenzimidazoles and related compds. as antithrombotics)

RN 253430-83-0 HCAPLUS

CN Pyrrolidine, 1-[amino[2-[[[4-(aminoiminomethyl)phenyl]amino]methyl]-1-methyl-1H-benzimidazol-5-yl]acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

## ● HCl

IT 253431-62-8P 253431-65-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amidinophenylaminomethylbenzimidazoles and related compds. as antithrombotics)

RN 253431-62-8 HCAPLUS

CN Pyrrolidine, 1-[amino[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]acetyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & NH_2 \\ \hline N - C - CH - \\ \hline \end{array} \begin{array}{c} N \\ \hline \end{array} \begin{array}{c} CN \\ \hline \end{array}$$

RN 253431-65-1 HCAPLUS

CN Pyrrolidine, 1-[2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & Me \\ \hline \\ N & C & C \\ \hline \\ H_2N & N \\ \hline \\ Me \end{array}$$

=> FIL REGISTRY

COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION
51.46 230.03

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE TOTAL

ENTRY SESSION
-4 00 -4 0

CA SUBSCRIBER PRICE -4.00 -4.00

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STRUCTURE FILE UPDATES: 13 FEB 2008 HIGHEST RN 1003293-96-6
DICTIONARY FILE UPDATES: 13 FEB 2008 HIGHEST RN 1003293-96-6

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> Uploading C:\Program Files\Stnexp\Queries\10560771a.str

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chain nodes :
12  13  14  15
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  16  17  18
chain bonds :
4-13  9-12  12-13  12-15  13-14
ring bonds :
1-2  1-5  2-3  3-4  4-5  6-7  6-11  6-18  7-8  7-16  8-9  9-10  10-11  16-17  17-18
exact/norm bonds :
1-2  1-5  2-3  3-4  4-5  4-13  6-7  6-11  6-18  7-8  7-16  8-9  9-10  9-12  10-11
12-13  12-15  13-14  16-17  17-18
isolated ring systems :
containing 1 : 6 :
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G1:0, S, N, NH

G2:CH2,CH,CF2,CF3

G3:CH2, CF2, CF3, SO2, SO3H, S

Match level :

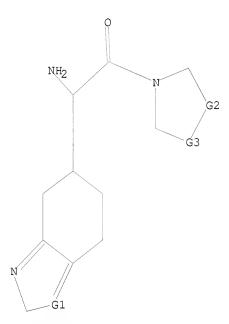
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L6 STRUCTURE UPLOADED

=> d 16

L6 HAS NO ANSWERS

L6 STR



G1 O, S, N, NH

G2 CH2, CH, CF2, CF3

G3 CH2, CF2, CF3, SO2, SO3H, S

Structure attributes must be viewed using STN Express query preparation.

=> s 16

SAMPLE SEARCH INITIATED 11:06:33 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 9 TO 360 PROJECTED ANSWERS: 0 TO 0

L7 0 SEA SSS SAM L6

=> s 16 sss full

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FULL SCREEN SEARCH COMPLETED - 161 TO ITERATE

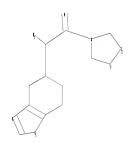
100.0% PROCESSED 161 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

L8 0 SEA SSS FUL L6

=>

Uploading C:\Program Files\Stnexp\Queries\10560771b.str



chain nodes :
12 13 14 15
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 16 17 18
chain bonds :
4-13 9-12 12-13 12-15 13-14
ring bonds :
1-2 1-5 2-3 3-4 4-5 6-7 6-11 6-18 7-8

 $1-2 \quad 1-5 \quad 2-3 \quad 3-4 \quad 4-5 \quad 6-7 \quad 6-11 \quad 6-18 \quad 7-8 \quad 7-16 \quad 8-9 \quad 9-10 \quad 10-11 \quad 16-17 \quad 17-18$ 

G1:0, S, N, NH

G2:CH2,CH,CF2,CF3

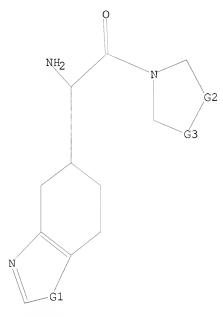
G3:CH2, CF2, CF3, SO2, SO3H, S

Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:Atom 17:Atom 18:Atom

L9 STRUCTURE UPLOADED

=> d 19 L9 HAS NO ANSWERS L9 STR



G1 O, S, N, NH

G2 CH2, CH, CF2, CF3

G3 CH2, CF2, CF3, SO2, SO3H, S

Structure attributes must be viewed using STN Express query preparation.

=> s 19

SAMPLE SEARCH INITIATED 11:11:29 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED

9 ITERATIONS

1 ANSWERS

02/14/2008

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*
PROJECTED ITERATIONS: 9 TO 360
PROJECTED ANSWERS: 1 TO 80

L10 1 SEA SSS SAM L9

=> s 19 sss full

FULL SEARCH INITIATED 11:11:36 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 161 TO ITERATE

100.0% PROCESSED 161 ITERATIONS 25 ANSWERS

SEARCH TIME: 00.00.01

L11 25 SEA SSS FUL L9

=> FIL HCAPLUS

COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
SINCE FILE TOTAL
ENTRY SESSION
359.94
589.97

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE TOTAL
ENTRY SESSION

CA SUBSCRIBER PRICE

0.00 -4.00

FILE 'HCAPLUS' ENTERED AT 11:11:41 ON 14 FEB 2008
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FILE COVERS 1907 - 14 Feb 2008 VOL 148 ISS 7 FILE LAST UPDATED: 13 Feb 2008 (20080213/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 111 L12 6 L11

=> s 112 and py<=2003 23976331 PY<=2003 L13 5 L12 AND PY<=2003

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=> s 112 and dipeptidyl peptidase
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          14336 PEPTIDASE
           4930 PEPTIDASES
          16580 PEPTIDASE
                   (PEPTIDASE OR PEPTIDASES)
           3041 DIPEPTIDYL PEPTIDASE
                   (DIPEPTIDYL(W)PEPTIDASE)
L14
              1 L12 AND DIPEPTIDYL PEPTIDASE
=> d 112 ibib abs hitstr tot
L12 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:1156435 HCAPLUS
                           142:86665
DOCUMENT NUMBER:
TITLE:
                           Cyclohexylglycine derivatives as dipeptidyl peptidase
                            IV inhibitors for the treatment or prevention of
                            diabetes and other dipeptidyl peptidase IV-associated
                            diseases
                            Edmondson, Scott D.; Mastracchio, Anthony; Parmee,
INVENTOR(S):
                           Emma R.
PATENT ASSIGNEE(S):
                           Merck & Co., Inc., USA
SOURCE:
                           PCT Int. Appl., 54 pp.
                           CODEN: PIXXD2
DOCUMENT TYPE:
                           Pat.ent.
LANGUAGE:
                           English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
                                                                          DATE
     PATENT NO.
                      KIND DATE
                                               APPLICATION NO.
                                                _____
                           ____
     _____

      WO 2004112701
      A2
      20041229
      WO 2004-US18718

      WO 2004112701
      A3
      20050210

                                                                         20040610
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
              CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
              GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
              LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
              NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
              TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
          RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
              AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
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              SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
              SN, TD, TG
     AU 2004249163
                           A1 20041229 AU 2004-249163 20040610
A1 20041229 CA 2004-2527806 20040610
A2 20060329 EP 2004-755091 20040610
     CA 2527806
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     CN 1809544 A 20060726 CN 2004-80016974 20040610
JP 2006528131 T 20061214 JP 2006-517334
                                               JP 2006-517234 20040610
IN 2005-DN5637 20051205
US 2005-560771 20051213
US 2003-479246P P 20030617
WO 2004-US18718 W 20040610
                           T 20061214
A 20080201
A1 20070125
     IN 2005DN05637
US 2007021477
PRIORITY APPLN. INFO.:
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OTHER SOURCE(S): MARPAT 142:86665

AB The invention discloses cyclohexylglycine derivs. which are inhibitors of dipeptidyl peptidase IV which are useful in the treatment or prevention of diseases in which dipeptidyl peptidase IV is involved, such as diabetes and particularly type 2 diabetes. The invention also discloses pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which the dipeptidyl peptidase IV enzyme is involved. Preparation of compds. and intermediates is described.

815580-74-6 815580-74-6D, derivs. 815580-75-7 815580-75-7D, derivs. 815580-76-8 815580-76-8D, derivs. 815580-77-9 815580-77-9D, derivs. 815580-79-1 815580-79-1D, derivs. 815580-80-4 815580-80-4D, derivs. 815580-87-1 815580-87-1D, derivs. 815580-88-2 815580-88-2D, derivs. 815580-89-3 815580-89-3D, derivs. 815580-90-6 815580-90-6D, derivs. 815580-91-7 815580-91-7D, derivs. 815580-92-8 815580-92-8D, derivs. 815580-93-9 815580-93-9D, derivs. 815580-94-0 815580-94-0D, derivs. 815580-95-1 815580-95-1D, derivs. 815580-96-2 815580-96-2D, derivs. 815580-97-3 815580-97-3D, derivs. 815580-98-4 815580-98-4D, derivs.

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cyclohexylglycine derivs. as dipeptidyl peptidase IV inhibitors for treatment or prevention of diabetes and other dipeptidyl peptidase IV-associated diseases)

RN 815580-74-6 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]- (9CI) (CA INDEX NAME)

RN 815580-74-6 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]- (9CI) (CA INDEX NAME)

RN 815580-75-7 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

RN 815580-75-7 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

RN 815580-76-8 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3,3difluoro- (9CI) (CA INDEX NAME)

RN 815580-76-8 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3,3-difluoro-(9CI) (CA INDEX NAME)

RN 815580-77-9 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-77-9 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzothiazoly1)acety1]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-79-1 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-79-1 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-80-4 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3,3-

difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-80-4 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3,3-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-87-1 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzoxazolyl)acetyl]- (9CI) (CA INDEX NAME)

RN 815580-87-1 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzoxazolyl)acetyl]- (9CI) (CA INDEX NAME)

RN 815580-88-2 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzoxazoly1)acety1]-3-fluoro-(9CI) (CA INDEX NAME)

RN 815580-88-2 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzoxazoly1)acety1]-3-fluoro-(9CI) (CA INDEX NAME)

RN

815580-89-3 HCAPLUS
Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzoxazoly1)acety1]-3,3-CN difluoro- (9CI) (CA INDEX NAME)

815580-89-3 HCAPLUS RN

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzoxazoly1)acety1]-3,3difluoro- (9CI) (CA INDEX NAME)

RN 815580-90-6 HCAPLUS

Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzoxazolyl)acetyl]-CN (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-90-6 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzoxazoly1)acety1]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-91-7 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzoxazolyl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-91-7 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzoxazolyl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-92-8 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzoxazoly1)acety1]-3,3-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-92-8 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzoxazolyl)acetyl]-3,3difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN

815580-93-9 HCAPLUS
Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-CN (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & NH_2 & H \\ \hline N & C - CH & N \end{array}$$

815580-93-9 HCAPLUS RN

Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-CN (9CI) (CA INDEX NAME)

RN 815580-94-0 HCAPLUS

Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3-CN fluoro- (9CI) (CA INDEX NAME)

RN 815580-94-0 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

RN 815580-95-1 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3,3-difluoro- (9CI) (CA INDEX NAME)

RN 815580-95-1 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3,3-difluoro-(9CI) (CA INDEX NAME)

RN 815580-96-2 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-96-2 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-97-3 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-97-3 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-98-4 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-

3,3-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-98-4 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3,3-difluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L12 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:2864 HCAPLUS

DOCUMENT NUMBER: 140:59935

TITLE: Preparation of crystalline (R)-2-(4-

amidinophenylaminomethyl)-1-methyl-5-(1-

(carboxymethylamino) -1 (pyrrolidinocarbonyl) -ethyl) -

benzimidazole esters and/or salts for use as

antithrombotic agents

INVENTOR(S): Linz, Guenter; Sieger, Peter; Schreiner, Gunnar; Rall,

Werner; Schmid, Rolf

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Gmbh & Co. Kg, Germany

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	ENT I	NO.			KIN	D	DATE			APPL	ICAT	ION :	NO.		D	ATE	
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WO	2004	0008	18		A1		2003	1231	1	WO 2	003-	EP63	17		2	0030	616
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	GM, HR, HU		HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	KΖ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NI,	NO,	NZ,	OM,
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KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
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             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                 20040108
                                             DE 2002-10227666
     DE 10227666
                           A1
                                                                     20020620
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                           A1
                                 20031231
                                             CA 2003-2485545
                                                                     20030616
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                           A1
                                 20040106
                                             AU 2003-237945
                                                                     20030616
     EP 1529035
                           A1
                                 20050511
                                             EP 2003-735629
                                                                     20030616
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     JP 2006508037
                           Т
                                 20060309
                                             JP 2004-514726
                                                                     20030616
     US 2004010026
                           A1
                                 20040115
                                             US 2003-463033
                                                                     20030617
     US 7169934
                           B2
                                 20070130
                                             US 2006-610187
     US 2007099974
                           A1
                                 20070503
                                                                     20061213
     US 7294721
                           B2
                                 20071113
PRIORITY APPLN. INFO.:
                                             DE 2002-10227666
                                                                     20020620
                                                                  Α
                                             US 2002-395188P
                                                                  Ρ
                                                                     20020711
                                             WO 2003-EP6317
                                                                  W
                                                                     20030616
                                                                  A3 20030617
                                             US 2003-463033
                         MARPAT 140:59935
OTHER SOURCE(S):
AR
     The invention relates to the crystalline forms of compds. (R)-2-(4-
     amidinophenylaminomethyl)-1-methyl-5-(1-(carboxymethylamino)-1-
     (pyrrolidinocarbonyl)-ethyl)-benzimidazole and monohydrochloride thereof,
     to methods for the production thereof, and to their use as medicaments having
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an antithrombotic action (no data). Thus, (R)-2-(4-

monohydrochloride forms. IT 253797-00-1

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation and x-ray crystallog. structure of 2-(4-amidinophenylaminomethyl))-1-methyl-5-(1-(carboxymethylamino)benzimidaz ole esters and/or salts for use as antithrombotic agents)

RN 253797-00-1 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

 $\label{lem:cyanophenylaminomethyl)-1-methyl-5-[1-amino-1-(pyrrolidineocarbonyl)-ethyl] benzimidazole was simultaneously N-alkylated and CN-reduced/aminated$ 

using BrCH2C(0)OCH2CH2CH3 in N-methylpyyolidinone, Pr acetate, and diisopropyethylamine; the resulting ester product was first isolated as the hydrochloride, and then as the 4-toluenesulfonic acid salt, which was deesterified to give the free base. The Et ester was similarly prepared

Crystal structure data were given for the free base and the

Absolute stereochemistry.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

INVENTOR(S):

ACCESSION NUMBER: 2004:2693 HCAPLUS

DOCUMENT NUMBER: 140:53413

TITLE: Benzimidazole derivatives for the treatment of

systemic inflammatory response syndrome Ries, Uwe; Wienen, Wolfgang; Schuly, Uwe

PATENT ASSIGNEE(S): Boehringer Ingelheim, Germany

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT:

PATENT	INFORMATION:

PAT	TENT :	MO.			KIN	D	DATE			APPI	JICAT	ION :	NO.		D	ATE	
WO	2004	0003:	10		A1	_	2003	1231	,	WO 2	2003-	EP63	 18		2	0030	616
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		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DΖ,	EC,	EE,	ES,	FΙ,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KΕ,	KG,	KΡ,	KR,	KΖ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MΧ,	ΜZ,	NI,	NO,	ΝZ,	OM,
		PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,
		TZ,	UA,	UG,	US,	UΖ,	VC,	VN,	YU,	ZA,	ZM,	ZW					
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
		KG,	KΖ,	MD,	RU,	ΤJ,	TM,	ΑT,	ΒE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FΙ,	FR,	GB,	GR,	HU,	ΙE,	ΙT,	LU,	MC,	ΝL,	PT,	RO,	SE,	SI,	SK,	TR,
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	ΤG
DE	1022	7668			A1		2004	0108		DE 2	2002-	1022	7668		2	0020	620
CA	2489	545			A1		2003	1231	1	CA 2	2003-	2489	545		2	0030	616
AU	2003	2789	45		A1		2004	0106		AU 2	2003-	2789	45		2	0030	616
EP	1517	687			A1		2005	0330		EP 2	2003-	7402	55		2	0030	616
EP	1517	687			В1		2007	0620									
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
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JP	2006	5146	03		Т						2004-						
AT	3650	38			Т						2003-						
ES	2289	305			Т3		2008	0201		ES 2	2003-	7402	55		2	0030	616
US	2004	0239	75		A1		2004	0205									
PRIORITY	Y APP	LN.	INFO	.:							2002-					0020	620
											2002-					0020	
										WO 2	2003-	EP63	18	1	₩ 2	0030	616

OTHER SOURCE(S): MARPAT 140:53413

AB The invention discloses the use of benzimidazole derivs. for producing a medicament used for treating the systemic inflammatory response syndrome and particularly sepsis. Preparation of (R)-2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(carboxymethylamino)-1-(pyrrolidinocarbonyl)ethyl]benzimidazol e hydrochloride is described.

IT 253797-00-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(benzimidazole derivs. for treatment of systemic inflammatory response syndrome)

RN 253797-00-1 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:467997 HCAPLUS

DOCUMENT NUMBER: 135:61338

TITLE: Preparation of 2-(4-amidinophenylaminomethyl)benzimida

zoles as antithrombotics

INVENTOR(S): Ries, Uwe; Kauffmann, Iris; Hauel, Norbert; Priepke,

Henning; Nar, Herbert; Stassen, Jean Marie; Wienen,

Wolfgang

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: Ger. Offen., 28 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	TENT	NO.			KIN		DATE			APP1	LICAT	ION	NO.		D.	ATE	
DE	1996	2329									 1999-					9991	
US	2001	0069	77		A1		2001	0705		US 2	2000-	7351	59		2	0001	212
US	6451	832			В2		2002	0917									
CA	2393	916			A1		2001	0705		CA 2	2000-	2393	916		2	0001	216
WO	2001	0478	96		A1		2001	0705		WO 2	2000-	EP12	841		2	0001	216
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EP	1244	636			A1		2002	1002		EP 2	2000-	9833	42		2	0001	216
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JP	2003	5191	29		$\mathbf{T}$		2003	0617		JP 2	2001-	5493	68		2	0001	216
MX	2002	PA06	299		Α		2002	1209		MX 2	2002-	PA62	99		2	0020	621
US	US 2003004356						2003	0102		US 2	2002-	1889	52		2	0020	703
US	6593	355			В2		2003	0715									
PRIORIT	PRIORITY APPLN. INFO.:									DE 3	1999-	1996	2329		A 1	9 <b>9</b> 91	223
										US 2	2000-	1751	63P		P 2	0000	107
										US 2	2000-	7351	59		<b>A</b> 1 2	0001	212
										WO 2	2000-	EP12	841	,	W 2	0001	216
OTHER S	THER SOURCE(S).						135.	6133	Ω								

OTHER SOURCE(S): MARPAT 135:61338

GΙ

RN

Title compds. [I; R1 = alkyl, fluoroalkyl, pyrrolidinocarbonylalkyl, 2,5-dihydropyrrolocarbonylalkyl, aminoalkyl, etc., R2 = alkyl; R3 = carbamidoyl, cyano, (substituted) oxadiazolyl, etc.] and stereoisomerics thereof were prepared .Thus, (R)-2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(ethoxycarbonylmethylamino)-1-[(R,S)-2-methylpyrrolidinocarbonyl]ethyl] benzimidazole dihydrochloride in H2O was stirred with NaOH for 45 min. at room temperature followed by addition of HCl up to pH = 3.5 to give 100% (R)-2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(carboxymethylamino)-1-[(R,S)-2-methylpyrrolidinocarbonyl]ethyl]benzimidazole dihydrochloride. Several I extended (doubled) the activated partial thromboplastin time (aPTT) with ED200 = 0.12-0.22  $\mu \rm M$ .

IT 253797-00-1P 345957-57-5P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amidinophenylaminomethylbenzimidazoles as antithrombotics) 253797-00-1 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 345957-57-5 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[1-methyl-2-[[[4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]amino]methyl]-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L12 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:34881 HCAPLUS

DOCUMENT NUMBER: 132:78556

TITLE: Preparation of amidinophenylaminomethylenzimidazoles

as antithrombotics.

Ries, Uwe; Kauffmann, Iris; Hauel, Norbert; Priepke, Henning; Nar, Herbert; Stassen, Jean Marie; Wienen, INVENTOR(S):

Wolfgang

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 140 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PAT	TENT	NO.			KIN	D	DATE			APPL	ICAT	ION :	NO.		D.	ATE	
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	2337							0113									
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	7630																
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					LV,							_					
EE	2001	0000	9		A		2002	0617	.7 EE 2001-9						1	9990	701
EΕ	4236				В1		2004	0216									

JP	2002519429	T	20020702	JΡ	2000-558106		19990701
AT	229511	T	20021215	AT	1999-932765		19990701
NZ	509625	A	20030829	NZ	1999-509625		19990701
SK	283744	В6	20031202	SK	2001-8		19990701
MX	2000PA12819	A	20040603	MX	2000-PA12819		20001219
IN	2000MN00760	A	20070615	IN	2000-MN760		20001221
ИО	2001000028	A	20010103	NO	2001-28		20010103
BG	105111	A	20011231	BG	2001-105111		20010103
HR	2001000007	A1	20011231	HR	2001-7		20010103
HR	2001000007	В1	20030430				
HK	1036976	A1	20041119	HK	2001-107199		20011015
PRIORITY	Y APPLN. INFO.:			DE	1998-19829964	Α	19980704
				DE	1998-19857202	Α	19981211
				DE	1999-19912690	Α	19990320
				WO	1999-EP4531	W	19990701

OTHER SOURCE(S): MARPAT 132:78556

GI

RN

$$R^2$$
 ABAr $R^4$   $R^3$ 

AB Title compds. [I; Ar = (substituted) phenylene, naphthylene, thienylene, thiazolylene, pyridinylene, pyrazinylene, pyrimidinylene, pyridazinylene; A = alkylene; B = O, S, CH2, CO, imino, SO, SO2; R2 = R1COX, etc.; R1 = alkoxy, amino, alkylamino, dialkylamino, etc.; X = cycloalkylene; R3 = H, alkyl; R4 = cyano, (substituted) amidino], were prepared Thus, 2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(pyrrolidin-1-ylcarbonyl)cyclopropyl]benzimidazole hydrochloride (multistep preparation given) showed aPTT (partial thrombin time) ED200 = 0.12 μM.

IT 253430-83-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amidinophenylaminomethylenzimidazoles as antithrombotics) 253430-83-0 HCAPLUS

CN Pyrrolidine, 1-[amino[2-[[[4-(aminoiminomethyl)phenyl]amino]methyl]-1methyl-1H-benzimidazol-5-yl]acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{NH} \\ & \text{O} & \text{NH}_2 \\ & \text{N} & \text{C} - \text{CH}_2 - \text{NH} \\ & & \text{N} \\ & & \text{Me} \end{array}$$

HC1

253431-62-8P 253431-65-1P 253796-87-1P ΙT

253797-00-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amidinophenylaminomethylenzimidazoles as antithrombotics)

RN

253431-62-8 HCAPLUS
Pyrrolidine, 1-[amino[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-CN benzimidazol-5-yl]acetyl]- (9CI) (CA INDEX NAME)

253431-65-1 HCAPLUS RN

Pyrrolidine, 1-[2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-CN benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{O} & \text{Me} \\ \hline \\ \text{N} & \text{C} - \text{C} \\ \hline \\ \text{H}_2 \text{N} \end{array} \begin{array}{c} \text{N} \\ \text{N} \\ \end{array} \begin{array}{c} \text{C} \text{N} \\ \text{N} \\ \end{array}$$

253796-87-1 HCAPLUS RN

Pyrrolidine, 1-[2-amino-2-[1-methyl-2-[[[4-(5-methyl-1,2,4-oxadiazol-3-methyl-1,2,4-oxadiazol-3-methyl-2-[]]CN yl)phenyl]amino]methyl]-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

RN 253797-00-1 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

## Absolute stereochemistry.

$$\begin{array}{c|c} & \text{Me} & \\ & \text{N} & \\ & \text{N} & \\ & \text{N} & \\ & \text{N} & \\ & \text{Me} & \\ &$$

L12 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:15648 HCAPLUS

DOCUMENT NUMBER: 132:64257

TITLE: Preparation of amidinophenylaminomethylbenzimidazoles

and related compounds as antithrombotics.

INVENTOR(S): Ries, Uwe; Kauffmann, Iris; Hauel, Norbert; Priepke,

Henning; Nar, Herbert; Stassen, Jean Marie; Wienen,

Wolfgang

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: Ger. Offen., 38 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND I	DATE	APPLICATION NO.	DATE
DE 19829964 US 6248770 TW 248435 CA 2337804 WO 2000001704	B1 2 B 2 A1 2	20000105 20010619 20060201 20000113 20000113	DE 1998-19829964 US 1999-338970 TW 1999-88110926 CA 1999-2337804 WO 1999-EP4531	19980704 19990624 19990629 19990701 19990701
WO 2000001704	A3 2	20000406		
			BB, BG, BR, BY, CA, CH,	
, ,	, , ,	, ,	GE, GH, GM, HR, HU, ID,	
JP, KE, K	G, KP, KR,	KZ, LC,	LK, LR, LS, LT, LU, LV,	MD, MG, MK,
MN, MW, M	X, NO, NZ,	PL, PT,	RO, RU, SD, SE, SG, SI,	SK, SL, TJ,
TM, TR, T	T, UA, UG,	UZ, VN,	YU, ZA, ZW	
RW: GH, GM, K	E, LS, MW,	SD, SL,	SZ, UG, ZW, AT, BE, CH,	CY, DE, DK,

										, NL,		SE,	BF,	ВJ,	CF,	CG,
		CM,	GA,	,	,					I, TD,						
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	763094			В2		2003			_	1000	1100	_		-	0000	
	9911826			A						1999-					9990	
	1095025			A2		2001		E	P	1999-	9327	65		Τ	9990	701
EP .	1095025		~**	B1		2002			~-							
	R: AT,		,				FR,	GB,	GR	, IT,	ьı,	LU,	ΝL,	SE,	MC,	PT,
mp.	•		LT,	LV,	ĿΙ,		0001			0001	1.40			1	0000	701
	200100148			T2		2001				2001-					9990	
	200100009	)		A		2002		E	ŀΕ	2001-	9			Τ	9990	70 I
	4236	1.0		B1		2004				2002	710			1	0000	701
	20020007			A2		2002		н	U	2002-	/10			1	9990	/ U I
	20020007: 20025194:			A3 T		2003		-	ъ	2000	E E O 1	0.0		1	0000	701
	20025194 <i>.</i> 229511	29		T		2002	_			2000- 1999-					9990' 9990'	
	1095025			T		2002				1999-				_	9990 9990	
	2188192			T3		2003				1999-					9990'	
	509625			13 A		2003				1999-					9990	
	283744			В6		2003				2001-		2 J			9990	
	200000762	2 /		A		2003		-		2001-	-				0001	
	200000702 2000PA128			A		2001				2000-					0001	
	20001A120 2000MN00	-		A		2007				2000-		-			0001	-
	200111000			A		2001				2001-		U			0010	
-	105111	_ 0		A		2001			-	2001-		11			0010	
_	200100000	17		A1		2001			-	2001-					0010	
	200100000			B1		2003				2001	•			_	0010	_ 00
	1036976	,		A1		2004		Н	K	2001-	1071	99		2	0011	015
PRIORITY		INFO	. :			_ 0 0 1				1998-					9980	
										1998-					9980	
								D	Ε	1998-	1985	7202			9981	
										1999-		_			9990.	
								W	Ю	1999-	EP45	31			9990	
OTUED COI	TIDCE / C \ .			MADD	ידי ע	132.	6125									

OTHER SOURCE(S): MARPAT 132:64257 GI

AB Title compds. [I; Ar = (substituted) phenylene, naphthylene, thienylene, thiazolylene, pyridinylene, etc.; A = alkylene; B = 0, S, CH2, CO, imino, sulfinyl, sulfonyl, etc.; R5 = R1COX; X = cycloalkylene; R1 = (substituted) (di)alkylamino, cycloalkyleneimino, morpholino, piperazino; R5 = H, alkyl; R7 = cyano, (substituted) amidino], were prepared Thus, 2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(pyrrolidin-1-ylcarbonyl)cyclopropyl]benzimidazole hydrochloride [prepared starting from 1-(4-chlorophenyl)-1-cyclopropanecarboxylic acid] showed aPTT (partial thrombin time) ED200 = 0.12  $\mu M$ .

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amidinophenylaminomethylbenzimidazoles and related compds. as antithrombotics)

RN 253430-83-0 HCAPLUS

CN Pyrrolidine, 1-[amino[2-[[[4-(aminoiminomethyl)phenyl]amino]methyl]-1-methyl-1H-benzimidazol-5-yl]acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & NH \\ \hline O & NH_2 \\ \hline N & C - CH \\ \hline & N \\ \hline & N \\ \hline \end{array}$$

#### ● HCl

IT 253431-62-8P 253431-65-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amidinophenylaminomethylbenzimidazoles and related compds. as antithrombotics)

RN 253431-62-8 HCAPLUS

CN Pyrrolidine, 1-[amino[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]acetyl]- (9CI) (CA INDEX NAME)

RN 253431-65-1 HCAPLUS

CN Pyrrolidine, 1-[2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & Me \\ \hline N & C - C \\ \hline H_2N & N \\ \hline \end{array}$$

## => d 113 ibib abs hitstr tot

L13 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:2864 HCAPLUS

DOCUMENT NUMBER: 140:59935

TITLE: Preparation of crystalline (R)-2-(4amidinophenylaminomethyl)-1-methyl-5-(1-

(carboxymethylamino) -1 (pyrrolidinocarbonyl) -ethyl) -

benzimidazole esters and/or salts for use as

antithrombotic agents

Linz, Guenter; Sieger, Peter; Schreiner, Gunnar; Rall, INVENTOR(S):

Werner; Schmid, Rolf

Boehringer Ingelheim Pharma Gmbh & Co. Kg, Germany PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Pat.ent. LANGUAGE: German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA:	TENT		KIN	D	DATE				ICAT	-	-		D.	ATE				
WO	2004	0008	 18		A1	_	2003	1231							2	0030	 616 ∢	<
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		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NI,	NO,	NZ,	OM,	
							SC,											
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	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,	
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		FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,	
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	ΤG	
DE	DE 10227666			A1		2004	0108		DE 2	002-	1022	7666		2	0020	620		
	2485																	<
AU	2003	2379	45		A1		2004	0106		AU 2	003-	2379	45		2	0030	616	
EP	1529	035			A1		2005	0511		EP 2	-600	7356	29		2	0030	616	
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		ΙE,	SI,	LT,	LV,	FΙ,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK		
	2006						2006	0309		JP 2	004-	5147	26		2	0030	616	
US	2004	0100	26		A1		2004	0115		US 2	-600	4630	33		2	0030	617	
US	7169	934			В2		2007	0130										
US	2007	0999	74		A1		2007	0503		US 2	006-	6101	87		2	0061	213	
US	7294	721			В2		2007	1113										
RIORIT	Y APP	LN.	INFO	.:									7666			0020		
									US 2	002-	3951	88P		P 2	0020	711		
										WO 2	003-	EP63	17	1	W 2	0030	616	
										US 2	-800	4630	33		A3 2	0030	617	
HER SO	JUBUE.	191.			MARI	DΔT	140.	59931	5									

OTHER SOURCE(S): MARPAT 140:59935

The invention relates to the crystalline forms of compds. (R)-2-(4amidinophenylaminomethyl)-1-methyl-5-(1-(carboxymethylamino)-1-(pyrrolidinocarbonyl)-ethyl)-benzimidazole and monohydrochloride thereof, to methods for the production thereof, and to their use as medicaments having an antithrombotic action (no data). Thus, (R)-2-(4cyanophenylaminomethyl)-1-methyl-5-[1-amino-1-(pyrrolidineocarbonyl)ethyl]benzimidazole was simultaneously N-alkylated and CN-reduced/aminated

using BrCH2C(0)OCH2CH2CH3 in N-methylpyyolidinone, Pr acetate, and diisopropyethylamine; the resulting ester product was first isolated as the hydrochloride, and then as the 4-toluenesulfonic acid salt, which was deesterified to give the free base. The Et ester was similarly prepared Crystal structure data were given for the free base and the monohydrochloride forms.

IT 253797-00-1

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation and x-ray crystallog. structure of 2-(4-amidinophenylaminomethyl))-1-methyl-5-(1-(carboxymethylamino)benzimidaz ole esters and/or salts for use as antithrombotic agents)

RN 253797-00-1 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:2693 HCAPLUS

DOCUMENT NUMBER: 140:53413

TITLE: Benzimidazole derivatives for the treatment of

systemic inflammatory response syndrome Ries, Uwe; Wienen, Wolfgang; Schuly, Uwe

PATENT ASSIGNEE(S): Boehringer Ingelheim, Germany

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

INVENTOR(S):

PAT	ENT	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D.	ATE	
WO	2004	0003			A1	_	2003	 1231	,	 WO 2		 EP63			2	0030	616 <
	W:	ΑE,	AG,	AL,	AM,	AT,	ΑU,	AZ,	BA,	BB,	ВG,	BR,	BY,	BZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FΙ,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MΖ,	NΙ,	NO,	NZ,	OM,
		PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	ΤJ,	TM,	TN,	TR,	TT,
		TZ,	UA,	UG,	US,	UΖ,	VC,	VN,	YU,	ZA,	ZM,	ZW					
	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ΖW,	AM,	ΑZ,	BY,
		KG,	ΚZ,	MD,	RU,	ΤJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FΙ,	FR,	GB,	GR,	HU,	ΙE,	ΙΤ,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GO,	GW,	ML,	MR,	NE,	SN,	TD,	TG

	1022 2489 2003	545	45		A1 A1 A1	2004 2003 2004	1231	CA :	2002- 2003- 2003-	24895	45		2	0020 0030 0030	616	<
EP	1517	687			A1	2005	0330	EP :	2003-	74025	5		2	0030	616	
EP	1517	687			В1	2007	0620									
	R:	ΑT,	BE,	CH,	DE,	DK, ES,	FR,	GB, GR	, IT,	LI,	LU,	NL,	SE,	MC,	PT,	
		ΙE,	SI,	LT,	LV,	FI, RO,	MK,	CY, AL	, TR,	BG,	CZ,	EE,	HU,	SK		
JP	2006	5146	03		T	2006	0511	JP :	2004-	51472	27		2	0030	616	
AT	3650	38			T	2007	0715	AT :	2003-	74025	5		2	0030	616	
ES	2289	305			Т3	2008	0201	ES :	2003-	74025	5		2	0030	616	
US	2004	0239	75		A1	2004	0205	US :	2003-	60005	55		2	0030	620	
PRIORIT	Y APP	LN.	INFO	. :				DE :	2002-	10227	668		A 2	0020	620	
								US :	2002-	40016	6P	]	P 2	0020	801	
								WO :	2003-	EP631	. 8	1	W 2	0030	616	

OTHER SOURCE(S): MARPAT 140:53413

AB The invention discloses the use of benzimidazole derivs. for producing a medicament used for treating the systemic inflammatory response syndrome and particularly sepsis. Preparation of (R)-2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(carboxymethylamino)-1-(pyrrolidinocarbonyl)ethyl]benzimidazol e hydrochloride is described.

IT 253797-00-1P

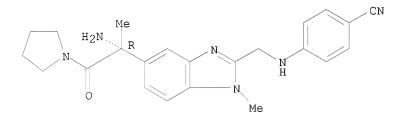
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(benzimidazole derivs. for treatment of systemic inflammatory response syndrome)

RN 253797-00-1 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:467997 HCAPLUS

DOCUMENT NUMBER: 135:61338

TITLE: Preparation of 2-(4-amidinophenylaminomethyl)benzimida

zoles as antithrombotics

INVENTOR(S): Ries, Uwe; Kauffmann, Iris; Hauel, Norbert; Priepke,

Henning; Nar, Herbert; Stassen, Jean Marie; Wienen,

Wolfgang

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: Ger. Offen., 28 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PA:	PATENT NO.					D	DATE			APPI	LICAT	ION	NO.		D	ATE		
	1996 2001						2001				 1999- 2000-						 223 <- 212 <-	
US	6451	832			В2		2002	0917					_					
	2393				A1		2001	0705		CA 2	2000-	2393	916		2	0001	216 <-	
WO	2001	0478	96		A1		2001	0705		WO 2	2000-	EP12	841		2	0001	216 <-	
	W:	ΑE,	AG,	AL,	AM,	AT	AU,	AZ,	BA,	BB,	, BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
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		HU,	ID,	IL,	IN,	IS	JP,	KE,	KG,	KP,	, KR,	KZ,	LC,	LK,	LR,	LS,	LT,	
		LU,	LV,	MA,	MD,	MG	MK,	MN,	MW,	MX,	, MZ,	NO,	NZ,	PL,	PT,	RO,	RU,	
		SD,	SE,	SG,	SI,	SK	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	
		YU,	ZA,	ZW			•	•	·		•	•	•	·	•	•	•	
	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	
		DE,	DK,	ES,	FI,	FR	GB,	GR,	IE,	IT,	, LU,	MC,	NL,	PT,	SE,	TR,	BF,	
		ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	, MR,	NE,	SN,	TD,	TG			
EP	1244	636	•		A1		2002	1002	·	EP 2	2000-	9833	42	·	2	0001	216 <-	
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							RO,											
JP	2003	5191	29		$\mathbf{T}$		2003	0617		JP 2	2001-	5493	68		2	0001	216 <-	
																	621 <-	
US	2003	0043	56		A1		2003	0102		US 2	2002-	1889	52		2	0020	703 <-	
US	6593	355			В2		2003	0715										
PRIORIT	Y APP	LN.	INFO	.:						DE 3	1999-	1996	2329		A 1	9991	223	
										US 2	2000-	1751	63P		P 2	0000	107	
									US 2	2000-	7351	59		A1 2	0001	212		
										WO 2	2000-	EP12	841		W 2	0001	216	
OTHER SO	SOURCE(S):			MAR	PAT	135:	6133	8										

GΙ

$$\begin{array}{c|c} R1 & \stackrel{N}{\longrightarrow} & \stackrel{H}{N} \\ & & \\ R2 & & \\ R3 & & \end{array}$$

AB Title compds. [I; R1 = alkyl, fluoroalkyl, pyrrolidinocarbonylalkyl, 2,5-dihydropyrrolocarbonylalkyl, aminoalkyl, etc., R2 = alkyl; R3 = carbamidoyl, cyano, (substituted) oxadiazolyl, etc.] and stereoisomerics thereof were prepared .Thus, (R)-2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(ethoxycarbonylmethylamino)-1-[(R,S)-2-methylpyrrolidinocarbonyl]ethyl] benzimidazole dihydrochloride in H2O was stirred with NaOH for 45 min. at room temperature followed by addition of HCl up to pH = 3.5 to give 100% (R)-2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(carboxymethylamino)-1-[(R,S)-2-methylpyrrolidinocarbonyl]ethyl]benzimidazole dihydrochloride. Several I extended (doubled) the activated partial thromboplastin time (aPTT) with ED200 = 0.12-0.22  $\mu \rm M$ .

IT 253797-00-1P 345957-57-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amidinophenylaminomethylbenzimidazoles as antithrombotics)

RN 253797-00-1 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 345957-57-5 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[1-methy1-2-[[[4-(5-methy1-1,2,4-oxadiazol-3-y1)phenyl]amino]methyl]-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L13 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:34881 HCAPLUS

DOCUMENT NUMBER: 132:78556

TITLE: Preparation of amidinophenylaminomethylenzimidazoles

as antithrombotics.

INVENTOR(S): Ries, Uwe; Kauffmann, Iris; Hauel, Norbert; Priepke,

Henning; Nar, Herbert; Stassen, Jean Marie; Wienen,

Wolfgang

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 140 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000001704	A2	20000113	WO 1999-EP4531	19990701 <

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WO 2000001704
                                20000406
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         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
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PRIORITY APPLN. INFO.:
                                             DE 1998-19829964
                                                                 A 19980704
                                             DE 1998-19857202
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                                                                 A 19990320
                                             WO 1999-EP4531
                                                                 W
                                                                    19990701
```

OTHER SOURCE(S): MARPAT 132:78556 GI

Ι

$$R^2$$
 ABArR<sup>4</sup>  $N$ 

AB Title compds. [I; Ar = (substituted) phenylene, naphthylene, thienylene, thiazolylene, pyridinylene, pyrazinylene, pyrimidinylene, pyridazinylene; A = alkylene; B = O, S, CH2, CO, imino, SO, SO2; R2 = R1COX, etc.; R1 = alkoxy, amino, alkylamino, dialkylamino, etc.; X = cycloalkylene; R3 = H, alkyl; R4 = cyano, (substituted) amidino], were prepared Thus, 2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(pyrrolidin-1-ylcarbonyl)cyclopropyl]benzimidazole hydrochloride (multistep preparation given) showed aPTT (partial thrombin time) ED200 = 0.12 μM.

IT 253430-83-0P

02/14/2008

RN

RN

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amidinophenylaminomethylenzimidazoles as antithrombotics) 253430-83-0 HCAPLUS

CN Pyrrolidine, 1-[amino[2-[[[4-(aminoiminomethyl)phenyl]amino]methyl]-1-methyl-1H-benzimidazol-5-yl]acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{NH} \\ & \text{O} \\ & \text{N} \\ & \text{C} \\ & \text{CH}_2 \\ & \text{N} \\ & \text{Me} \end{array}$$

### ● HCl

IT 253431-62-8P 253431-65-1P 253796-87-1P 253797-00-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amidinophenylaminomethylenzimidazoles as antithrombotics) 253431-62-8 HCAPLUS

CN Pyrrolidine, 1-[amino[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]acetyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & NH_2 \\ \hline N & C - CH \\ \hline \end{array} \begin{array}{c} N \\ \hline \end{array} \begin{array}{c} CH_2 - NH \\ \hline \end{array} \begin{array}{c} CN \\ \hline \end{array}$$

RN 253431-65-1 HCAPLUS

CN Pyrrolidine, 1-[2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
O & Me \\
N - C - C \\
H_2N & N
\end{array}$$

$$\begin{array}{c}
N - CH_2 - NH \\
Me
\end{array}$$

RN 253796-87-1 HCAPLUS

CN Pyrrolidine, 1-[2-amino-2-[1-methyl-2-[[[4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]amino]methyl]-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

RN 253797-00-1 HCAPLUS

CN Pyrrolidine, 1-[(2R)-2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L13 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:15648 HCAPLUS

DOCUMENT NUMBER: 132:64257

TITLE: Preparation of amidinophenylaminomethylbenzimidazoles

and related compounds as antithrombotics.

INVENTOR(S): Ries, Uwe; Kauffmann, Iris; Hauel, Norbert; Priepke,

Henning; Nar, Herbert; Stassen, Jean Marie; Wienen,

Wolfgang

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: Ger. Offen., 38 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19829964	A1	20000105	DE 1998-19829964	19980704 <
US 6248770	В1	20010619	US 1999-338970	19990624 <
TW 248435	В	20060201	TW 1999-88110926	19990629
CA 2337804	A1	20000113	CA 1999-2337804	19990701 <
WO 2000001704	A2	20000113	WO 1999-EP4531	19990701 <
WO 2000001704	A3	20000406		

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PRIORITY APPLN. INFO.:
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                        MARPAT 132:64257
OTHER SOURCE(S):
GΙ
```

AB Title compds. [I; Ar = (substituted) phenylene, naphthylene, thienylene, thiazolylene, pyridinylene, etc.; A = alkylene; B = 0, S, CH2, CO, imino, sulfinyl, sulfonyl, etc.; R5 = R1COX; X = cycloalkylene; R1 = (substituted) (di)alkylamino, cycloalkyleneimino, morpholino, piperazino; R5 = H, alkyl; R7 = cyano, (substituted) amidino], were prepared Thus, 2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(pyrrolidin-1-ylcarbonyl)cyclopropyl]benzimidazole hydrochloride [prepared starting from

1-(4-chloropheny1)-1-cyclopropanecarboxylic acid] showed aPTT (partial thrombin time) ED200 = 0.12  $\mu M$ .

IT 253430-83-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amidinophenylaminomethylbenzimidazoles and related compds. as antithrombotics)

RN 253430-83-0 HCAPLUS

CN Pyrrolidine, 1-[amino[2-[[[4-(aminoiminomethyl)phenyl]amino]methyl]-1-methyl-1H-benzimidazol-5-yl]acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

#### HCl

IT 253431-62-8P 253431-65-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of amidinophenylaminomethylbenzimidazoles and related compds. as antithrombotics)

RN 253431-62-8 HCAPLUS

CN Pyrrolidine, 1-[amino[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]acetyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & NH_2 \\ \hline N & C - CH \\ \hline \end{array} \begin{array}{c} N \\ N \end{array} \begin{array}{c} CH_2 - NH \\ \hline \end{array} \begin{array}{c} CN \\ N \end{array}$$

RN 253431-65-1 HCAPLUS

CN Pyrrolidine, 1-[2-amino-2-[2-[[(4-cyanophenyl)amino]methyl]-1-methyl-1H-benzimidazol-5-yl]-1-oxopropyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} O & Me \\ \hline N & C & C \\ \hline H_2N & N \\ \hline \end{array}$$

## => d 114 ibib abs hitstr tot

L14 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:1156435 HCAPLUS

DOCUMENT NUMBER: 142:86665

TITLE: Cyclohexylglycine derivatives as dipeptidyl

peptidase IV inhibitors for the treatment or prevention of diabetes and other dipeptidyl

peptidase IV-associated diseases

INVENTOR(S): Edmondson, Scott D.; Mastracchio, Anthony; Parmee,

Emma R.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

P	'ΑΤ	ENT 1	NO.			KIN		DATE			APPI	LICAT	ION :	NO.		D.	ATE	
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A	U	2004	2491	63		A1		2004	1229		AU 2	2004-	2491	63		2	0040	610
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E	P	1638	950			A2		2006	0329		EP 2	2004-	7550	91		2	0040	610
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_	CN 1809544 JP 2006528131											2006-						
	IN 2005DN05637																	
	US 2007021477																	
	OS 2007021477 IORITY APPLN. INFO.:										US 2	2003- 2004-1	4792	46P	1	P 2		617

MARPAT 142:86665 OTHER SOURCE(S): The invention discloses cyclohexylqlycine derivs. which are inhibitors of dipeptidyl peptidase IV which are useful in the treatment or prevention of diseases in which dipeptidyl peptidase IV is involved, such as diabetes and particularly type 2 diabetes. The invention also discloses pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which the dipeptidyl peptidase IV enzyme is involved. Preparation of compds. and intermediates is described. ΙT 815580-74-6 815580-74-6D, derivs. 815580-75-7 815580-75-7D, derivs. 815580-76-8 815580-76-8D , derivs. 815580-77-9 815580-77-9D, derivs. 815580-79-1 815580-79-1D, derivs. 815580-80-4 815580-80-4D, derivs. 815580-87-1 815580-87-1D , derivs. 815580-88-2 815580-88-2D, derivs. 815580-89-3 815580-89-3D, derivs. 815580-90-6 815580-90-6D, derivs. 815580-91-7 815580-91-7D , derivs. 815580-92-8 815580-92-8D, derivs. 815580-93-9 815580-93-9D, derivs. 815580-94-0 815580-94-0D, derivs. 815580-95-1 815580-95-1D , derivs. 815580-96-2 815580-96-2D, derivs. 815580-97-3 815580-97-3D, derivs. 815580-98-4 815580-98-4D, derivs. RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (cyclohexylglycine derivs. as dipeptidyl peptidase IV inhibitors for treatment or prevention of diabetes and other dipeptidyl peptidase IV-associated diseases) 815580-74-6 HCAPLUS RN CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]- (9CI) (CA INDEX NAME)

RN 815580-74-6 HCAPLUS
CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]- (9CI)
(CA INDEX NAME)

RN 815580-75-7 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

RN 815580-75-7 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

RN 815580-76-8 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3,3difluoro- (9CI) (CA INDEX NAME)

RN 815580-76-8 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3,3difluoro- (9CI) (CA INDEX NAME)

RN 815580-77-9 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-77-9 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzothiazoly1)acety1]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-79-1 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-79-1 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-80-4 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3,3-

difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-80-4 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzothiazolyl)acetyl]-3,3-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-87-1 HCAPLUS

RN 815580-87-1 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzoxazolyl)acetyl]- (9CI) (CA INDEX NAME)

RN 815580-88-2 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzoxazolyl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

RN 815580-88-2 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzoxazoly1)acety1]-3-fluoro-(9CI) (CA INDEX NAME)

RN

815580-89-3 HCAPLUS
Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzoxazoly1)acety1]-3,3-CN difluoro- (9CI) (CA INDEX NAME)

815580-89-3 HCAPLUS RN

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-5-benzoxazoly1)acety1]-3,3difluoro- (9CI) (CA INDEX NAME)

RN 815580-90-6 HCAPLUS

Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzoxazolyl)acetyl]-CN (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-90-6 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzoxazoly1)acety1]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-91-7 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzoxazolyl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-91-7 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzoxazolyl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-92-8 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzoxazoly1)acety1]-3,3-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-92-8 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-5-benzoxazolyl)acetyl]-3,3difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN

815580-93-9 HCAPLUS
Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-CN (9CI) (CA INDEX NAME)

815580-93-9 HCAPLUS RN

Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-CN (9CI) (CA INDEX NAME)

RN 815580-94-0 HCAPLUS

Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3-CN fluoro- (9CI) (CA INDEX NAME)

RN 815580-94-0 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

RN 815580-95-1 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3,3-difluoro-(9CI) (CA INDEX NAME)

RN 815580-95-1 HCAPLUS

CN Pyrrolidine, 1-[amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3,3-difluoro-(9CI) (CA INDEX NAME)

RN 815580-96-2 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-96-2 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-97-3 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-97-3 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3-fluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-98-4 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-

# 3,3-difluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 815580-98-4 HCAPLUS

CN Pyrrolidine, 1-[(2S)-amino(4,5,6,7-tetrahydro-1H-benzimidazol-5-yl)acetyl]-3,3-difluoro-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

=> log y COST IN U.S. DOLLARS	SINCE FILE	TOTAL
FULL ESTIMATED COST	ENTRY 81.54	SESSION 671.51
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.60	-13.60

STN INTERNATIONAL LOGOFF AT 11:15:04 ON 14 FEB 2008